DETAILED ACTION

Response to the Amendment

The Amendment filed on 7/28/2008 in response to the previous Non-Final Office Action (4/29/2008) is acknowledged and has been entered.

Claim 1 is currently pending and under consideration.

Rejections Maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 remains rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Meyerson et al. (The EMBO Journal 1992; 11: 2909-2917) in view of Yamamoto et al. (International Journal of Oncology 1998; 13: 233-239).

Meyerson et al. teach the identification of a novel family of human cdc2-realted protein kinases. In particular, Meyerson et al. teach a peptide referred to as PCTAIRE-3 which appears to have 100% sequence identity to the claimed sequence of SEQ ID NO: 4 and methods of using the a nucleic acid which encodes said polypeptide for screening (see sequence comparison below, page 2911, Figure 1 and page 2913, Figure 5). Moreover, Meyerson et al. teach that the nucleic acid encoding said peptide is present in MCF-7 human breast adenocarcinoma cell lines (figure 4).

Meyerson et al. does not explicitly teach a method of screening for biologically active agents that modulate PCTAIRE-3 comprising combining a candidate biologically acitve agent with PCTAIRE-3.

Yamamoto et al. teach that cyclin dependent kinases such as cdk2 and cdc2 are overexpressed in colon carcinoma (page 233, 2nd column, 2nd full paragraph). However, Yamamoto

et al. teaches that it remains to be clarified whether cdk2 and cdc2 levels increase in tumorogenesis (page 233, 2nd column, 2nd full paragraph). Hence, Yamamoto et al. teach a method of determining role of cdk2/cdc2 in colon cancer cells comprising contacting said cancer cells with a specific inhibitor of cdk2 and cdc2 and determining the effects on the cells, wherein the inhibitor the growth of the cancer cells (page 236, 1st column, Growth inhibition of colon carcinoma cells with butyrolactone I). Thus, the reference teaches that inhibition of cdk2/cdc2 using a certain drug or antisense nucleotide may be a useful strategy against colon cancer.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the reference so as to determine the role of the peptide as taught by Meyerson et al. in MCF-7 human breast adenocarcinoma cells lines by using a suspected inhibitor of cdc2 in view of the teachings of Yamamoto et al. One would have been motivated to do so because as taught by Yamamoto et al., successful inhibition of a cancer related protein having a role in tumorogenesis leads to a useful strategy for treatment of the disease. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by determining the role of the peptide as taught by Meyerson et al. in MCF-7 human breast adenocarcinoma cells lines by using a suspected inhibitor of cdc2 in view of the teachings of Yamamoto et al., one would clarify the role of PCTAIRE-3 in breast cancer.

In response to this rejection, Applicants contend that the primary reference, Meyerson et al. teaches the genetic sequence of a number of protein kinases based on their structural relation to p34CDC2. In particular, Applicants contend that while the reference notes expression of PCTAIRE-3 in MCF-7 cell line, there is no indication in the reference that the polypeptide is useful in screening methods involving combining a candidate biologically active agent with a peptide. Moreover, Applicants assert that while the reference indicates some of the polypeptide (e.g., cdk2, cdk3, PSSALRE and PLSTIRE but not PCTAIRE-3) were used in complemementation assays by transformation into yeast cells, there is no teaching of screening assays aimed at determining the activity of a candidate agent that modulates the activity of the polypeptide encoded by SEQ IDNO: 4. Applicants further assert that while Yamamoto et al .teaches the use of a known inhibitor of cdk2/cdc2, and the use of such a known inhibitor to determine the effect of specific inhibition on growth and apoptosis of colon cancer cell lines, the reference fails to remedy the deficiencies of the primary reference. Additionally, Applicants contend that, in contrast to Yamamoto et al., the present

claims are directed to identifying an agent that modulates the function of PCTK3, which is distinct from assays performed with agents having known specific inhibitory activity. Applicants also note that PCTK3 is biologically distinct from interacting kinase cdk2/ckc2. For example, Applicants contend that while there is some structural similarity, the sequence differences are significant, for example as shown in Figure 1 of Myerson et al. Thus, Applicants assert that one of skill in the art would not utilize a specific inhibitor of cdk2/cdc2 in a screening assay developed for PCTK3.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner acknowledges and does not dispute Applicants assertions that Meyerson et al .do not teach using the polypeptide in a screening method involving combining a candidate biologically active agent with a peptide or Applicants assertions that Yamamoto et al. teaches the use of a known inhibitor of cdk2/cdc2. However, the Examiner recognizes that it must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references, which make up the state of the art with regard to the claimed invention. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). The examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). For example, motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (National Steel Car v. Canadian Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). In the instant case, the Examiner recognizes Meyerson et al. teach the identification of a novel family of human cdc2-realted protein kinases. In particular,

Meyerson et al. teach a peptide referred to as PCTAIRE-3 which appears to have 100% sequence identity to the claimed sequence of SEQ ID NO: 4 and methods of using the a nucleic acid which encodes said polypeptide for screening (see sequence comparison below, page 2911, Figure 1 and page 2913, Figure 5). Moreover, Meyerson et al. teach that the nucleic acid encoding said peptide is present in MCF-7 human breast adenocarcinoma cell lines (figure 4). The knowledge of one of ordinary skill in the art at the time the invention was made recognize that cdc2 related kinases have separate and distinct function in the control of cell growth, division, differentiation and/or development (Myerson et al., page 2915, 2nd column, 2nd full paragraph). For example, in view of Yamamoto et al., those of skill in the art recognize that both cdk2/cdc2 are upregulated in focal cancer and inhibition of cdk2/cdc2 inhibits the proliferation of carcinoma cells. Thus, in view of the teachings of the prior art, one would be motivated to identify inhibitors of PCTAIRE-3 and determine the effects of inhibition PCTAIRE-3 in MCF-7 human breast adenocarcinoma cell lines which have been shown to express PCTAIRE-3.

Therefore, No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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